This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

(Currently amended) A compound, comprising: a targeting moiety and a chelator,
wherein the targeting moiety is bound to the chelator, is a indazole nonpeptide, and
binds to a receptor that is upregulated during angiogenesis and the compound has 0-1
linking groups between the targeting moiety and chelator

wherein the indazole nonpeptide targeting moiety is represented by (Q)_d wherein Q is independently a a compound of Formula (Ia) or (Ib):

$$\begin{array}{c|c}
R^{1d} & X^{4d} & R^{11d} \\
\hline
X^{3d} & X^{3d} & Y^{d} \\
\hline
X^{1d} & X^{2d} & Y^{d} \\
\hline
R^{10d} & X^{10d} & X^{10d} \\
\hline
\end{array}$$

(Ia)

or pharmaceutically acceptable salt form thereof wherein:

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

X^{1d} is CH, C-W^d-X^d-Y^d, or C bonded to the linking group;

X^{2d} is CH, or C- Wd- Xd- Yd;

X3d is CR11d, or C- Wd- Xd- Yd;

x4d is CR11d;

provided that when R1d is R1de then one of X1d and X2d is C- Wd- Xd- Yd, and when R10d is R1de then X3d is C- Wd- Xd- Yd;

R1d is R1de, C1-C6 alkyl substituted with 0-1 R15d or 0-1 R21d, C3-C6 alkenyl substituted with 0-1 R15d or 0-1 R21d, C3-C7 cycloalkyl substituted with 0-1 R15d or 0-1 R21d, C4-C11 cycloalkylalkyl substituted with 0-1 R15d or 0-1 R21d, aryl substituted with 0-1 R15d or 0-2 R11d or 0-1 R21d, or aryl(C1-C6 alkyl)- substituted with 0-1 R15d or 0-2 R11d or 0-1 R21d;

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

Office Action Dated: June 16, 2006

R1de is

$$-U^{d}(NR^{6d}) \xrightarrow{B^{d}} U^{d}(NR^{6d}) \xrightarrow{P^{d}} B^{1d}$$

$$- U^{d}(NR^{6d}) - V^{d} - V^{d}$$

$$- U^{d}(NR^{6d}) - V^{d} - V^{d}$$

$$- U^{d}(NR^{6d}) - \int_{D^{d}}^{K^{d}} F^{d}$$

$$U^{d} - U^{d}$$

$$V^{d} - V^{d}$$

$$\sum_{F^d-E^d}^{N}$$
 or $\sum_{F^d}^{N}$

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

A^d and B^d are independently -CH₂-, -O-, -N(R^{2d})-, or -C(=O)-;

A1d and B1d are independently -CH2- or -N(R3d)-;

 D^{d} is $-N(R^{2d})$ -, -O-, -S-, -C(=O)- or -SO₂-;

 $E^{d}-F^{d}$ is $-C(R^{4d})=C(R^{5d})-$, $-N=C(R^{4d})-$, $-C(R^{4d})=N-$, or $-C(R^{4d})2C(R^{5d})2-$;

Jd, Kd, Ld and Md are independently

-C(R^{4d})-, -C(R^{5d})- or -N-, provided that at least one of Jd, Kd, Ld and Md is not -N-;

- R^{2d} is H, C₁-C₆ alkyl, (C₁-C₆ alkyl)carbonyl, (C₁-C₆ alkoxy)carbonyl; (C₁-C₆ alkyl)aminocarbonyl, C₃-C₆ alkenyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, heteroaryl(C₁-C₆ alkyl)carbonyl, heteroarylcarbonyl, aryl(C₁-C₆ alkyl)-, (C₁-C₆ alkyl)carbonyl-, arylcarbonyl, C₁-C₆ alkylsulfonyl, arylsulfonyl, aryl(C₁-C₆ alkyl)sulfonyl, heteroarylsulfonyl, heteroaryl(C₁-C₆ alkyl)sulfonyl, aryloxycarbonyl, or aryl(C₁-C₆ alkoxy)carbonyl, wherein said aryl groups are substituted with 0-2 substituents selected from the group consisting of C₁-C₄ alkyl, C₁-C₄ alkoxy, halo, CF₃, and nitro:
- R^{3d} is H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, or heteroaryl(C₁-C₆ alkyl)-;

DOCKET NO.: DM-6999 (BMS-2594) **Application No.:** 10/770,380 REPLY FILED UNDER EXPEDITED

Office Action Dated: June 16, 2006 PROCEDURE PURSUANT TO 37 CFR § 1.116

PATENT

R^{4d} and R^{5d} are independently H, C₁-C₄ alkoxy, NR^{2d}R^{3d}, halogen, NO₂, CN, CF₃, C₁-C6 alkyl, C3-C6 alkenyl, C3-C7 cycloalkyl, C4-C11 cycloalkylalkyl, aryl, aryl(C1-C6 alkyl)-, (C1-C6 alkyl)carbonyl, (C1-C6 alkoxy)carbonyl, or arylcarbonyl, or

alternatively, when substituents on adjacent atoms, R^{4d} and R^{5d} can be taken together with the carbon atoms to which they are attached to form a 5-7 membered carbocyclic or 5-7 membered heterocyclic aromatic or non-aromatic ring system, said carbocyclic or heterocyclic ring being optionally substituted with 0-2 groups selected from the group consisting of C1-C4 alkyl, C1-C4 alkoxy, halo, cyano, amino, CF3, and NO2;

Ud is:

-(CH₂)_nd₋,

 $-(CH_2)_n d(CR^{7d}=CR^{8d})(CH_2)_m d_{-1}$

 $-(CH_2)_n d(C \equiv C)(CH_2)_m d$

-(CH2)t^dQ^d (CH2)m^d-,

 $-(CH_2)_n dO(CH_2)_m d_{-}$

 $-(CH_2)_n dN(R^{6d})(CH_2)_m d_{-1}$

 $-(CH_2)_n dC(=O)(CH_2)_m d_{-1}$

 $-(CH_2)_n d(C=O)N(R^{6d})(CH_2)_m d$

 $-(CH_2)_n dN(R^{6d})(C=O)(CH_2)_m d$ -, and

 $-(CH_2)_n dS(O)_p d(CH_2)_m d-$;

wherein one or more of the methylene groups in U^d is optionally substituted with R^{7d};

Qd is 1,2-cycloalkylene, 1,2-phenylene, 1,3-phenylene, 1,4-phenylene, 2,3-pyridinylene, 3,4pyridinylene, 2,4-pyridinylene, or 3,4-pyridazinylene;

DOCKET NO.: DM-6999 (BMS-2594)
Application No.: 10/770,380
Application Dated: June 16, 2006
PROCEDURE PURSUANT TO
37 CFR § 1.116

R^{6d} is H, C₁-C₄ alkyl, or benzyl;

R^{7d} and R^{8d} are independently H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, or heteroaryl(C₀-C₆ alkyl)-;

- R10d is H, R1de, C1-C4 alkoxy substituted with 0–1 R21d, N(R6d)2, halogen, NO2, CN, CF3, CO2R17d, C(=O)R17d, CONR17dR20d, -SO2R17d, -SO2NR17dR20d, C1-C6 alkyl substituted with 0-1 R15d or 0-1 R21d, C3-C6 alkenyl substituted with 0-1 R15d or 0-1 R21d, C3-C7 cycloalkyl substituted with 0-1 R15d or 0-1 R21d, aryl substituted with 0-1 R15d or 0-2 R11d or 0-1 R21d, or aryl(C1-C6 alkyl)-substituted with 0-1 R15d or 0-2 R11d or 0-1 R21d;
- R^{10de} is H, C₁-C₄ alkoxy substituted with 0–1 R^{21d}, N(R^{6d})₂, halogen, NO₂, CN, CF₃, CO₂R^{17d}, C(=O)R^{17d}, CONR^{17d}R^{20d}, -SO₂R^{17d}, -SO₂NR^{17d}R^{20d}, C₁-C₆ alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₃-C₆ alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₃-C₇ cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d}, or aryl(C₁-C₆ alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d};
- R^{11d} is H, halogen, CF₃, CN, NO₂, hydroxy, NR^{2d}R^{3d}, C₁-C₄ alkyl substituted with 0-1

 R^{21d}, C₁-C₄ alkoxy substituted with 0-1 R^{21d}, aryl substituted with 0-1 R^{21d},

 aryl(C₁-C₆ alkyl)- substituted with 0-1 R^{21d}, (C₁-C₄ alkoxy)carbonyl substituted

 with 0-1 R^{21d}, (C₁-C₄ alkyl)carbonyl substituted with 0-1 R^{21d},

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

<u>C1-C4</u> alkylsulfonyl substituted with 0-1 R^{21d}, or <u>C1-C4</u> alkylaminosulfonyl substituted with 0-1 R^{21d};

wd is:

 $-(C(R^{12d})_2)_q dC(=O)N(R^{13d})$ -, or

 $-C(=O)-N(R^{13d})-(C(R^{12d})_2)_qd$ -;

 X^{d} is $-C(R^{12d})(R^{14d})-C(R^{12d})(R^{15d})-:$ or

alternatively, Wd and Xd can be taken together to be

$$(CH_2)_q^{d}C(=0) - N N - R^{18d}$$

R^{12d} is H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₇ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, (C₁-C₄ alkyl)carbonyl, aryl, or aryl(C₁-C₆ alkyl)-;

R^{13d} is H, C₁-C₆ alkyl, C₃-C₇ cycloalkylmethyl, or aryl(C₁-C₆ alkyl)-;

R^{14d} is:

H, C1-C6 alkylthio(C1-C6 alkyl)-, aryl(C1-C10 alkylthioalkyl)-, aryl(C1-C10 alkoxyalkyl)-, C1-C10 alkyl, C1-C10 alkoxyalkyl, C1-C6 hydroxyalkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C3-C10 cycloalkylalkyl, aryl(C1-C6 alkyl)-, heteroaryl(C1-C6 alkyl)-, aryl, heteroaryl, C02R^{17d}, C(=O)R^{17d}, or CONR^{17d}R^{20d}, provided that any of the above alkyl, cycloalkyl, aryl or heteroaryl groups may be unsubstituted or substituted independently with 1 R^{16d} or 1-2 R^{11d};

Application No.: 10/770,380 **Office Action Dated:** June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

R^{15d} is:

H, R^{16d}, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxyalkyl, C₁-C₁₀ alkylaminoalkyl, C₁-C₁₀ dialkylaminoalkyl, (C₁-C₁₀ alkyl)carbonyl, aryl(C₁-C₆ alkyl)carbonyl, C₁-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl, C₃-C₁₀ cycloalkylalkyl, aryl(C₁-C₆ alkyl)-, heteroaryl(C₁-C₆ alkyl)-, aryl, heteroaryl, C₂R^{17d}, C(=O)R^{17d}, C(=O)R^{17d}, CONR^{17d}R^{20d}, SO₂R^{17d}, or SO₂NR^{17d}R^{20d}, provided that any of the above alkyl, cycloalkyl, aryl or heteroaryl groups may be unsubstituted or substituted independently with 1-2 R^{11d};

Yd is:

-COR^{19d}, -SO₃H, -PO₃H, tetrazolyl, -CONHNHSO₂CF₃, -CONHSO₂R^{17d}, CONHSO₂NHR^{17d}, -NHCOCF₃, -NHCONHSO₂R^{17d}, -NHSO₂R^{17d}, -OPO₃H₂, OSO₃H, -PO₃H₂, -SO₃H, -SO₂NHCOR^{17d}, -SO₂NHCO₂R^{17d},

M N N CF3 OF HOO;

R^{16d} is:

 $-N(R^{20}d)-C(=O)-O-R^{17}d$

 $-N(R^{20d})-C(=O)-R^{17d}$

 $-N(R^{20d})-C(=O)-NH-R^{17d}$

-N(R^{20d})SO₂-R^{17d}, or

-N(R^{20d})SO₂-NR^{20d}R^{17d};

DOCKET NO.: DM-6999 (BMS-2594) **Application No.:** 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

R^{17d} is:

C1-C10 alkyl optionally substituted with a bond to the linking group, C3-C11 cycloalkyl optionally substituted with a bond to the linking group, aryl(C1-C6 alkyl)-optionally substituted with a bond to the linking group, (C1-C6 alkyl)aryl optionally substituted with a bond to the linking group, heteroaryl(C1-C6 alkyl)- optionally substituted with a bond to the linking group, (C1-C6 alkyl)heteroaryl optionally substituted with a bond to the linking group, biaryl(C1-C6 alkyl)- optionally substituted with a bond to the linking group, heteroaryl optionally substituted with a bond to the linking group, heteroaryl optionally substituted with a bond to the linking group, biaryl optionally substituted with a bond to the linking group, biaryl optionally substituted with a bond to the linking group, or a bond to the linking group, wherein said aryl, biaryl or heteroaryl groups are also optionally substituted with 0-3 substituents selected from the group consisting of C1-C4 alkyl, C1-C4 alkoy, aryl, heteroaryl, halo, cyano, amino, CF3, and NO2;

R^{18d} is:

<u>-H,</u>

 $-C(=O)-O-R^{17d}$

 $-C(=O)-R^{17d}$

 $-C(=O)-NH-R^{17d}$,

-SO₂-R^{17d}, or

-SO2-NR20dR17d;

R^{19d} is hydroxy, C₁-C₁₀ alkyloxy, C₃-C₁₁ cycloalkyloxy, aryloxy, aryl(C₁-C₆ alkoxy)-, C₃-C₁₀ alkylcarbonyloxyalkyloxy, C₃-C₁₀ alkoxycarbonyloxyalkyloxy, C₅-C₁₀ cycloalkylcarbonyloxyalkyloxy,

C5-C10 cycloalkoxycarbonyloxyalkyloxy, C5-C10 cycloalkoxycarbonylalkyloxy,

C7-C11 aryloxycarbonylalkyloxy, C8-C12 aryloxycarbonyloxyalkyloxy,

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

<u>C8-C12</u> arylcarbonyloxyalkyloxy, <u>C5-C10</u> alkoxyalkylcarbonyloxyalkyloxy, <u>C5-C10</u> (5-alkyl-1,3-dioxa-cyclopenten-2-one-yl)methyloxy, <u>C10-C14</u> (5-aryl-1,3-dioxa-cyclopenten-2-one-yl)methyloxy, or (R^{11d})(R^{12d})N-(C1-C10 alkoxy)-;

 R^{20d} is H, C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl, C_4 - C_{11} cycloalkylalkyl, aryl, aryl(C_1 - C_6 alkyl)-, or heteroaryl(C_1 - C_6 alkyl)-:

R^{21d} is COOH or NR^{6d}2;

d is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

with the following provisos:

- $\frac{d}{(1)}\frac{d}{t}, \frac{d}{n}, \frac{d}{m} \frac{d}{and} \frac{d}{q} \frac{d}{are \ chosen \ such \ that \ the \ number \ of \ atoms \ connecting \ R^{1d} \ and \ Y}{d} \ is \ in \\ \frac{the \ range \ of \ 10\text{-}14; \ and}{d}$
- (2) $\frac{d}{n}$ and $\frac{d}{m}$ are chosen such that the value of $\frac{d}{n}$ plus $\frac{d}{n}$ is greater than one unless $\frac{d}{n}$ is $\frac{d}{n}$ $\frac{d}{n}$
- 2-57. Canceled.

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

58. (New) A compound according to Claim 1, wherein the receptor is the integrin $\alpha_V \beta_3$ or $\alpha_V \beta_5$ and the compound is of the formula:

$$(Q)_d$$
- L_n - C_h or $(Q)_d$ - L_n - $(C_h)_d$ '

wherein, Q is independently a compound of Formula (Ia) or (Ib):

$$R^{1d}$$
 X^{4d}
 X^{3d}
 X^{3d}
 X^{2d}
 X^{1d}
 X^{2d}
 X^{1d}
 X^{2d}
 X^{1d}

(Ia)

$$R^{1de}$$
 N
 X^{4d}
 X^{3d}
 X^{3d}
 X^{2d}
 X^{2d}

or pharmaceutically acceptable salt form thereof wherein:

X^{1d} is CH, C- Wd- Xd- Yd, or C bonded to Ln;

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

X^{2d} is CH, or C- W^d- X^d- Y^d; X^{3d} is CR^{11d}, or C- W^d- X^d- Y^d; X^{4d} is CR^{11d};

provided that when R^{1d} is R^{1de} then one of X^{1d} and X^{2d} is C- W^d- X^d- Y^d, and when R^{10d} is R^{1de} then X^{3d} is C- W^d- X^d- Y^d;

 R^{1d} is R^{1de} , C_1 - C_6 alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_6 alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_7 cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_4 - C_{11} cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} , or aryl(C_1 - C_6 alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} ;

R1de is

REPLY FILED UNDER EXPEDITED Office Action Dated: June 16, 2006 PROCEDURE PURSUANT TO 37 CFR § 1.116

PATENT

$$-U^{d}(NR^{6d}) \xrightarrow{B^{d}} U^{d}(NR^{6d}) \xrightarrow{R^{d}} U^{d}(NR^{6d}) \xrightarrow{B^{1d}} U^{d}(NR^{6d})$$

$$- U^{d}(NR^{6d}) - V^{d} - V^{d}$$

$$- U^{d}(NR^{6d}) - V^{d} - V^{d} - V^{d}(NR^{6d}) - V^{d} - V^{d}(NR^{6d}) - V^{d} - V^{$$

$$- U^{d}(NR^{6d}) - \int_{D^{d}}^{N} \int_{E^{d}}^{F^{d}}$$

$$- U^{d}(NR^{6d}) - \int_{D^{d}}^{N} \int_{F^{d}}^{R^{2d}N}$$

$$- U^{d}(NR^{6d}) - \int_{D^{d}}^{N} \int_{F^{d}}^{R^{2d}N} \int_{F^{d}}^{N} \int_{F^{d}}^{R^{2d}N} \int_{F^{d}}^{N} \int_{F^{d}}^{N}$$

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

 A^d and B^d are independently -CH2-, -O-, -N(R^{2d})-, or -C(=O)-;

A^{1d} and B^{1d} are independently -CH₂- or -N(R^{3d})-;

 D^{d} is $-N(R^{2d})$ -, -O-, -S-, -C(=O)- or $-SO_{2}$ -;

 E^{d} - F^{d} is $-C(R^{4d})$ = $C(R^{5d})$ -, -N= $C(R^{4d})$ -, $-C(R^{4d})$ =N-, or $-C(R^{4d})$ 2 $C(R^{5d})$ 2-;

J^d, K^d, L^d and M^d are independently -C(R^{4d})-, -C(R^{5d})- or -N-, provided that at least one of J^d, K^d, L^d and M^d is not -N-;

R^{2d} is H, C₁-C₆ alkyl, (C₁-C₆ alkyl)carbonyl, (C₁-C₆ alkoxy)carbonyl; (C₁-C₆ alkyl)aminocarbonyl, C₃-C₆ alkenyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, heteroaryl(C₁-C₆ alkyl)carbonyl, heteroarylcarbonyl, aryl(C₁-C₆ alkyl)-, (C₁-C₆ alkyl)carbonyl-, arylcarbonyl, C₁-C₆ alkylsulfonyl, arylsulfonyl, aryl(C₁-C₆ alkyl)sulfonyl, heteroarylsulfonyl, heteroaryl(C₁-C₆ alkyl)sulfonyl, aryloxycarbonyl, or aryl(C₁-C₆ alkoxy)carbonyl, wherein said aryl groups are substituted with 0-2 substituents selected from the group consisting of C₁-C₄ alkyl, C₁-C₄ alkoxy, halo, CF₃, and nitro;

R^{3d} is H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, or heteroaryl(C₁-C₆ alkyl)-;

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

R^{4d} and R^{5d} are independently H, C₁-C₄ alkoxy, NR^{2d}R^{3d}, halogen, NO₂, CN, CF₃, C₁-C₆ alkyl, C₃-C₆ alkenyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, (C₁-C₆ alkyl)carbonyl, (C₁-C₆ alkoxy)carbonyl, or arylcarbonyl, or

alternatively, when substituents on adjacent atoms, R^{4d} and R^{5d} can be taken together with the carbon atoms to which they are attached to form a 5-7 membered carbocyclic or 5-7 membered heterocyclic aromatic or non-aromatic ring system, said carbocyclic or heterocyclic ring being optionally substituted with 0-2 groups selected from the group consisting of C1-C4 alkyl, C1-C4 alkoxy, halo, cyano, amino, CF3, and NO2;

Ud is:

 $-(CH_2)_n d_{-}$

 $-(CH_2)_n d(CR^{7d} = CR^{8d})(CH_2)_m d_{-1}$

 $-(CH_2)_n d(C \equiv C)(CH_2)_m d_{-n}$

 $-(CH_2)_t dQ^d (CH_2)_m d_-,$

 $-(CH_2)_n dO(CH_2)_m d_{-}$

 $-(CH_2)_n dN(R^{6d})(CH_2)_m d_{-1}$

 $-(CH_2)_n dC (=O)(CH_2)_m d_-,$

 $-(CH_2)_n d(C=O)N(R^{6d})(CH_2)_m d_-$

-(CH₂) $_n$ dN(R^{6d})(C=O)(CH₂) $_m$ d-, and

 $\hbox{-(CH$_2$)$}_n\hbox{d}{\rm S(O)}_p\hbox{d}{\rm (CH$_2$)$}_m\hbox{d-;}$

wherein one or more of the methylene groups in U^d is optionally substituted with R^{7d} ;

Q^d is 1,2-cycloalkylene, 1,2-phenylene, 1,3-phenylene, 1,4-phenylene, 2,3-pyridinylene, 3,4-pyridinylene, 2,4-pyridinylene, or 3,4-pyridazinylene;

DOCKET NO.: DM-6999 (BMS-2594) **Application No.:** 10/770,380 **Office Action Dated:** June 16, 2006

R^{6d} is H, C₁-C₄ alkyl, or benzyl;

- R^{7d} and R^{8d} are independently H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, or heteroaryl(C₀-C₆ alkyl)-;
- $R^{10d} \text{ is H, R}^{1de}, C_1\text{-}C_4 \text{ alkoxy substituted with 0--1 R}^{21d}, N(R^{6d})_2, \text{ halogen, NO}_2, CN, \\ CF_3, CO_2R^{17d}, C(=0)R^{17d}, CONR^{17d}R^{20d}, -SO_2R^{17d}, \\ -SO_2NR^{17d}R^{20d}, C_1\text{-}C_6 \text{ alkyl substituted with 0-1 R}^{15d} \text{ or 0-1 R}^{21d}, C_3\text{-}C_6 \\ \text{alkenyl substituted with 0-1 R}^{15d} \text{ or 0-1 R}^{21d}, C_3\text{-}C_7 \text{ cycloalkyl substituted with 0-1 R}^{15d} \text{ or 0-1 R}^{21d}, \\ R^{15d} \text{ or 0-1 R}^{21d}, C_4\text{-}C_{11} \text{ cycloalkylalkyl substituted with 0-1 R}^{15d} \text{ or 0-1 R}^{21d}, \\ \text{aryl substituted with 0-1 R}^{15d} \text{ or 0-2 R}^{11d} \text{ or 0-1 R}^{21d}, \text{ or aryl(C1-C6 alkyl)-substituted with 0-1 R}^{15d} \text{ or 0-2 R}^{11d} \text{ or 0-1 R}^{21d}; \\ \end{cases}$
- $R^{10\text{de}} \text{ is H, C1-C4 alkoxy substituted with 0-1 R}^{21\text{d}}, N(R^{6\text{d}})_2, \text{ halogen, NO2, CN, CF3,} \\ CO_2R^{17\text{d}}, C(=0)R^{17\text{d}}, CONR^{17\text{d}}R^{20\text{d}}, -SO_2R^{17\text{d}}, -SO_2NR^{17\text{d}}R^{20\text{d}}, C_1\text{-C6 alkyl} \\ \text{substituted with 0-1 R}^{15\text{d}} \text{ or 0-1 R}^{21\text{d}}, C_3\text{-C6 alkenyl substituted with 0-1 R}^{15\text{d}} \text{ or 0-1 R}^{21\text{d}}, C_3\text{-C7 cycloalkyl substituted with 0-1 R}^{15\text{d}} \text{ or 0-1 R}^{21\text{d}}, C_4\text{-C11} \\ \text{cycloalkylalkyl substituted with 0-1 R}^{15\text{d}} \text{ or 0-1 R}^{21\text{d}}, \text{ aryl substituted with 0-1 R}^{15\text{d}} \\ \text{ or 0-2 R}^{11\text{d}} \text{ or 0-1 R}^{21\text{d}}, \text{ or aryl(C1-C6 alkyl)- substituted with 0-1 R}^{15\text{d}} \text{ or 0-2 R}^{11\text{d}}, C_4\text{-C11}} \\ \text{R}^{11\text{d}} \text{ or 0-1 R}^{21\text{d}}, \text{ or aryl(C1-C6 alkyl)- substituted with 0-1 R}^{15\text{d}} \text{ or 0-2 R}^{11\text{d}}, C_4\text{-C11}} \\ \text{R}^{11\text{d}} \text{ or 0-1 R}^{21\text{d}}, \text{ or aryl(C1-C6 alkyl)- substituted with 0-1 R}^{15\text{d}} \text{ or 0-2}} \\ \text{R}^{11\text{d}} \text{ or 0-1 R}^{21\text{d}}, C_4\text{-C11}} \\ \text{R}^{11\text{d}} \text{ or 0$
- R^{11d} is H, halogen, CF3, CN, NO₂, hydroxy, NR^{2d}R^{3d}, C₁-C₄ alkyl substituted with 0-1 R^{21d}, C₁-C₄ alkoxy substituted with 0-1 R^{21d}, aryl substituted with 0-1 R^{21d}, aryl(C₁-C₆ alkyl)- substituted with 0-1 R^{21d}, (C₁-C₄ alkoxy)carbonyl substituted with 0-1 R^{21d}, (C₁-C₄ alkyl)carbonyl substituted with 0-1 R^{21d},

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

C₁-C₄ alkylsulfonyl substituted with 0-1 R^{21d}, or C₁-C₄ alkylaminosulfonyl substituted with 0-1 R^{21d};

wd is:

$$-(C(R^{12d})_2)_q dC(=O)N(R^{13d})$$
-, or

$$-C(=O)-N(R^{13d})-(C(R^{12d})_2)_q^{d}$$
;

 X^d is $-C(R^{12d})(R^{14d})-C(R^{12d})(R^{15d})-$; or alternatively, W^d and X^d can be taken together to be

$$-$$
 (CH₂)_qdC (=0) -N N-R^{18d}

R^{12d} is H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₇ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, (C₁-C₄ alkyl)carbonyl, aryl, or aryl(C₁-C₆ alkyl)-;

R^{13d} is H, C₁-C₆ alkyl, C₃-C₇ cycloalkylmethyl, or aryl(C₁-C₆ alkyl)-;

R^{14d} is:

H, C1-C6 alkylthio(C1-C6 alkyl)-, aryl(C1-C10 alkylthioalkyl)-, aryl(C1-C10 alkoxyalkyl)-, C1-C10 alkyl, C1-C10 alkoxyalkyl, C1-C6 hydroxyalkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C3-C10 cycloalkylalkyl, aryl(C1-C6 alkyl)-, heteroaryl(C1-C6 alkyl)-, aryl, heteroaryl, C02R^{17d}, C(=O)R^{17d}, or CONR^{17d}R^{20d}, provided that any of the above alkyl, cycloalkyl, aryl or heteroaryl groups may be unsubstituted or substituted independently with 1 R^{16d} or 1-2 R^{11d};

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

R15d is:

H, R^{16d}, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxyalkyl, C₁-C₁₀ alkylaminoalkyl, C₁-C₁₀ dialkylaminoalkyl, (C₁-C₁₀ alkyl)carbonyl, aryl(C₁-C₆ alkyl)carbonyl, C₁-C₁₀ alkenyl, C₁-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl, C₃-C₁₀ cycloalkylalkyl, aryl(C₁-C₆ alkyl)-, heteroaryl(C₁-C₆ alkyl)-, aryl, heteroaryl, CO₂R^{17d}, C(=O)R^{17d}, C(ONR^{17d}R^{20d}, SO₂R^{17d}, or SO₂NR^{17d}R^{20d}, provided that any of the above alkyl, cycloalkyl, aryl or heteroaryl groups may be unsubstituted or substituted independently with 1-2 R^{11d};

Yd is:

-COR 19d , -SO3H, -PO3H, tetrazolyl, -CONHNHSO2CF3, -CONHSO2R 17d , -CONHSO2NHR 17d , -NHCOCF3, -NHCONHSO2R 17d , -NHSO2R 17d , -OPO3H2, -OSO3H, -PO3H2, -SO3H, -SO2NHCOR 17d , -SO2NHCO2R 17d ,

R^{16d} is:

 $-N(R^{20d})-C(=O)-O-R^{17d}$

 $-N(R^{20d})-C(=O)-R^{17d}$

 $-N(R^{20d})-C(=O)-NH-R^{17d}$

 $-N(R^{20d})SO_2-R^{17d}$, or

-N(R²⁰d)SO₂-NR²⁰dR¹⁷d:

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

R17d is:

C1-C10 alkyl optionally substituted with a bond to L_n , C3-C11 cycloalkyl optionally substituted with a bond to L_n , aryl(C1-C6 alkyl)- optionally substituted with a bond to L_n , (C1-C6 alkyl)aryl optionally substituted with a bond to L_n , heteroaryl(C1-C6 alkyl)- optionally substituted with a bond to L_n , (C1-C6 alkyl)heteroaryl optionally substituted with a bond to L_n , biaryl(C1-C6 alkyl)- optionally substituted with a bond to L_n , heteroaryl optionally substituted with a bond to L_n , aryl optionally substituted with a bond to L_n , or a bond to L_n , wherein said aryl, biaryl or heteroaryl groups are also optionally substituted with 0-3 substituents selected from the group consisting of C1-C4 alkyl, C1-C4 alkoxy, aryl, heteroaryl, halo, cyano, amino, CF3, and NO2;

R18d is:

-H.

 $-C(=O)-O-R^{17d}$

 $-C(=O)-R^{17d}$,

 $-C(=O)-NH-R^{17d}$

 $-SO_2-R^{17}d$, or

 $-SO_2\text{-}NR^{20}d_R17d;$

R^{19d} is hydroxy, C₁-C₁₀ alkyloxy, C₃-C₁₁ cycloalkyloxy, aryloxy, aryl(C₁-C₆ alkoxy)-, C₃-C₁₀ alkylcarbonyloxyalkyloxy, C₃-C₁₀ alkoxycarbonyloxyalkyloxy, C₂-C₁₀ alkoxycarbonylalkyloxy, C₅-C₁₀ cycloalkylcarbonyloxyalkyloxy, C₅-C₁₀ cycloalkoxycarbonylalkyloxy, C₇-C₁₁ aryloxycarbonylalkyloxy, C₈-C₁₂ aryloxycarbonyloxyalkyloxy,

 $C8-C_{12} \ arylcarbonyloxyalkyloxy, \ C5-C_{10} \ alkoxyalkylcarbonyloxyalkyloxy,$

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

C5-C₁₀ (5-alkyl-1,3-dioxa-cyclopenten-2-one-yl)methyloxy, C₁₀-C₁₄ (5-aryl-1,3-dioxa-cyclopenten-2-one-yl)methyloxy, or (R^{11d})(R^{12d})N-(C₁-C₁₀ alkoxy)-;

 R^{20d} is H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, or heteroaryl(C₁-C₆ alkyl)-:

 R^{21d} is COOH or NR^{6d}_2 ;

$$is 0-4;$$

d' is 1-100

with the following provisos:

- (1) t^d , n^d , m^d and q^d are chosen such that the number of atoms connecting R^{1d} and Y^d is in the range of 10-14; and
- (2) n^d and m^d are chosen such that the value of n^d plus m^d is greater than one unless U^d is $-(CH_2)_t^d Q^d (CH_2)_m^d$ -;

 L_n is a linking group having the formula:

$$((W)_{h}-(CR^{6}R^{7})_{g})_{x}-(Z)_{k}-((CR^{6a}R^{7a})_{g}-(W)_{h})_{x};$$

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

W is independently selected at each occurrence from the group consisting of O, S, NH, NHC(=O), C(=O)NH, NR⁸C(=O), C(=O)N R⁸, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, SO₂NH, (OCH₂CH₂O)_S, (CH₂CH₂O)_S, (OCH₂CH₂O)_S, (CH₂CH₂O)_S, and (aa)_t;

aa is independently at each occurrence an amino acid;

- Z is aryl substituted with 0-3 R¹⁰, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁰, or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from the group consisting of N, S, and O and substituted with 0-3 R¹⁰;
- R^6 , R^6 a, R^7 , R^7 a, and R^8 are independently selected at each occurrence from the group consisting of H, =O, COOH, SO3H, PO3H, C1-C5 alkyl substituted with 0-3 R^{10} , aryl substituted with 0-3 R^{10} , benzyl substituted with 0-3 R^{10} , C1-C5 alkoxy substituted with 0-3 R^{10} , NHC(=O)R¹¹, C(=O)NHR¹¹, NHC(=O)NHR¹¹, NHR¹¹, R^{11} , and a bond to Ch;
- R^{10} is independently selected at each occurrence from the group consisting of a bond to C_h , C^{11} , C^{10} , C^{11} , C^{10} , C^{11} , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from the group consisting of C^{11} , and C^{11} , and C^{11} , C^{11} , and C^{11} , C^{11} , and C^{11} , and C^{11} , C^{11} , and C^{11} , C^{11} , and C^{11} , C^{11} , C^{11} , and C^{11} , and C^{11} , C^{11} , and C^{1
- R¹¹ is independently selected at each occurrence from the group consisting of H, alkyl substituted with 0-1 R¹², aryl substituted with 0-1 R¹², a 5-10 membered Page 22 of 51

DOCKET NO.: DM-6999 (BMS-2594) **Application No.:** 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹², C₃₋₁₀ cycloalkyl substituted with 0-1 R¹², polyalkylene glycol substituted with 0-1 R¹², carbohydrate substituted with 0-1 R¹², cyclodextrin substituted with 0-1 R¹², amino acid substituted with 0-1 R¹², polycarboxyalkyl substituted with 0-1 R¹², polyazaalkyl substituted with 0-1 R¹², peptide substituted with 0-1 R¹², wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to Ch;

R¹² is a bond to Ch;

k is 0, 1, or 2;

h is 0, 1, or 2;

h' is 0, 1, or 2;

g is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

g' is m 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

s is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

s' is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

s" is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

t is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

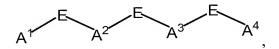
t' is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

x is 0, 1, 2, 3, 4, or 5;

x' is 0, 1, 2, 3, 4, or 5;

Ch is a metal bonding unit having a formula selected from the group consisting of:





Page 23 of 51

Application No.: 10/770,380

Office Action Dated: June 16, 2006

REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

A⁵

$$A^{8}$$
 A^{8}
 A^{8}

A¹, A², A³, A⁴, A⁵, A⁶, A⁷, and A⁸ are independently selected at each occurrence from the group consisting of NR¹³, NR¹³R¹⁴, S, SH, S(Pg), O, OH, PR¹³, PR¹³R¹⁴, $P(O)R^{15}R^{16}$, and a bond to L_n ;

E is a bond, CH, or a spacer group independently selected at each occurrence from the group consisting of C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, aryl substituted with 0-3 R¹⁷, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁷, heterocyclo-C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆₋₁₀ aryl-C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, C₁₋₁₀ alkyl-C₆₋₁₀ aryl- substituted with 0-3 R¹⁷, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from the group consisting of N, S, and O and substituted with $0-3 R^{17}$:

 R^{13} and R^{14} are each independently selected from the group consisting of a bond to L_n , hydrogen, C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, aryl substituted with 0-3 R¹⁷, C₁₋₁₀ cycloalkyl substituted with 0-3 R¹⁷, heterocyclo-C₁₋₁₀ alkyl substituted with DOCKET NO.: DM-6999 (BMS-2594)
Application No.: 10/770,380
Office Action Dated: June 16, 2006
PROCEDURE PURSUANT TO
37 CFR § 1.116

0-3 R¹⁷, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from consisting of N, S, and O, C6-10 aryl-C1-10 alkyl substituted with 0-3 R¹⁷, C1-10 alkyl-C6-10 aryl- substituted with 0-3 R¹⁷, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷, and an electron, provided that when one of R¹³ or R¹⁴ is an electron, then the other is also an electron;

alternatively, R^{13} and R^{14} combine to form = $C(R^{20})(R^{21})$;

R¹⁵ and R¹⁶ are each independently selected from the group consisting of a bond to L_n,
-OH, C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, C₁-C₁₀ alkyl substituted with 0-3 R¹⁷,
aryl substituted with 0-3 R¹⁷, C₃-10 cycloalkyl substituted with 0-3 R¹⁷,
heterocyclo-C₁-10 alkyl substituted with 0-3 R¹⁷, wherein the heterocyclo group is a
5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently
selected from N, S, and O, C₆-10 aryl-C₁-10 alkyl substituted with 0-3 R¹⁷, C₁-10
alkyl-C₆-10 aryl- substituted with 0-3 R¹⁷, and a 5-10 membered heterocyclic ring
system containing 1-4 heteroatoms independently selected from the group consisting
of N, S, and O and substituted with 0-3 R¹⁷;

 $R^{17} \text{ is independently selected at each occurrence from the group consisting of a bond to L_n, $$ =O, F, Cl, Br, I, -CF3, -CN, -CO_2R^{18}, -C(=O)R^{18}, -C(=O)N(R^{18})_2, -CHO, $$ -CH_2OR^{18}, -OC(=O)R^{18}, -OC(=O)OR^{18a}, -OR^{18}, -OC(=O)N(R^{18})_2, $$ -NR^{19}C(=O)R^{18}, -NR^{19}C(=O)OR^{18a}, -NR^{19}C(=O)N(R^{18})_2, -NR^{19}SO_2N(R^{18})_2, -NR^{19}SO_2R^{18a}, -SO_3H, -SO_2R^{18a}, -SR^{18}, -S(=O)R^{18a}, -SO_2N(R^{18})_2, -N(R^{18})_2, -NHC(=S)NHR^{18}, =NOR^{18}, NO_2, -C(=O)NHOR^{18}, -C(=O)NHNR^{18}R^{18a}, $$ Page 25 of 51$

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

-OCH₂CO₂H, 2-(1-morpholino)ethoxy, C₁-C₅ alkyl, C₂-C₄ alkenyl, C₃-C₆ cycloalkyl, C₃-C₆ cycloalkylmethyl, C₂-C₆ alkoxyalkyl, aryl substituted with 0-2 R¹⁸, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from the group consisting of N, S, and O;

 R^{18} , R^{18a} , and R^{19} are independently selected at each occurrence from the group consisting of a bond to L_n , H, C_1 - C_6 alkyl, phenyl, benzyl, C_1 - C_6 alkoxy, halide, nitro, cyano, and trifluoromethyl;

Pg is a thiol protecting group;

 R^{20} and R^{21} are independently selected from the group consisting of H, C₁-C₁₀ alkyl, -CN, -CO₂R²⁵, -C(=O)R²⁵, -C(=O)N(R²⁵)₂, C₂-C₁₀ 1-alkene substituted with 0-3 R²³, C₂-C₁₀ 1-alkyne substituted with 0-3 R²³, aryl substituted with 0-3 R²³, unsaturated 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from the group consisting of N, S, and O and substituted with 0-3 R²³, and unsaturated C₃-10 carbocycle substituted with 0-3 R²³;

alternatively, R^{20} and R^{21} , taken together with the divalent carbon radical to which they are attached form:

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

- R^{22} and R^{23} are independently selected from the group consisting of H, R^{24} , C_1 - C_{10} alkyl substituted with 0-3 R^{24} , C_2 - C_{10} alkenyl substituted with 0-3 R^{24} , C_2 - C_{10} alkynyl substituted with 0-3 R^{24} , aryl substituted with 0-3 R^{24} , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from the group consisting of N, S, and O and substituted with 0-3 R^{24} , and C_3 -10 carbocycle substituted with 0-3 R^{24} ;
- alternatively, R²², R²³ taken together form a fused aromatic or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from the group consisting of N, S, and O;

a and **b** indicate the positions of optional double bonds and **n** is 0 or 1;

- $R^{24} \text{ is independently selected at each occurrence from the group consisting of } = O, F, Cl, Br, I, -CF3, -CN, -CO2R^{25}, -C(=O)R^{25}, -C(=O)N(R^{25})2, -N(R^{25})3^+, -CH_2OR^{25}, -OC(=O)R^{25}, -OC(=O)OR^{25a}, -OR^{25}, -OC(=O)N(R^{25})2, -NR^{26}C(=O)R^{25}, -NR^{26}C(=O)R^{25a}, -NR^{26}C(=O)N(R^{25})2, -NR^{26}SO_2N(R^{25})2, -NR^{26}SO_2R^{25a}, -SO_3H, -SO_2R^{25a}, -SR^{25}, -S(=O)R^{25a}, -SO_2N(R^{25})2, -N(R^{25})2, -N(R^{25})2, =NOR^{25}, -C(=O)NHOR^{25}, -OCH_2CO_2H, and 2-(1-morpholino)ethoxy; and,$
- R²⁵, R^{25a}, and R²⁶ are each independently selected at each occurrence from the group consisting of hydrogen and C₁-C₆ alkyl.
- 59. (New) A compound according to Claim 58, wherein:

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

R^{1de} is:

$$- U^{d}(NR^{6d}) - V^{d} = K^{d}$$

$$- U^{d}(NR^{6d}) - V^{d} = K^{d}$$

$$- U^{d}(NR^{6d}) - V^{d} = K^{d}$$

$$-- U^{d}(NR^{6d}) - \int_{D^{d}}^{N} F^{d}$$

$$\downarrow D^{d}$$

 A^d and B^d are independently -CH2-, -O-, -N(R^2d)-, or -C(=O)-;

A^{1d} and B^{1d} are independently -CH₂- or -N(R^{3d})-;

DOCKET NO.: DM-6999 (BMS-2594) REPLY FILED UNDER EXPEDITED

PROCEDURE PURSUANT TO

37 CFR § 1.116

PATENT

 D^{d} is -N(R^{2d})-, -O-, -S-, -C(=O)- or -SO₂-;

Application No.: 10/770,380

Office Action Dated: June 16, 2006

 E^{d} - F^{d} is -C(R⁴d)=C(R⁵d)-, -N=C(R⁴d)-, -C(R⁴d)=N-, or -C(R⁴d)₂C(R⁵d)₂-;

- J^d , K^d , L^d and M^d are independently $C(R^{4d})$ -, $-C(R^{5d})$ or -N-, provided that at least one of J^{d} . K^{d} . L^{d} and M^{d} is not -N-;
- R^{2d} is H, C₁-C₆ alkyl, (C₁-C₆ alkyl)carbonyl, (C₁-C₆ alkoxy)carbonyl, C₁-C₆ alkylaminocarbonyl, C3-C6 alkenyl, C3-C7 cycloalkyl, C4-C11 cycloalkylalkyl, aryl, heteroaryl(C1-C6 alkyl)carbonyl, heteroarylcarbonyl, aryl(C1-C6 alkyl)-, (C1-C6 alkyl)carbonyl, arylcarbonyl, alkylsulfonyl, arylsulfonyl, aryl(C1-C6 alkyl)sulfonyl, heteroarylsulfonyl, heteroaryl(C₁-C₆ alkyl)sulfonyl, aryloxycarbonyl, or aryl(C₁-C₆ alkoxy)carbonyl, wherein said aryl groups are substituted with 0-2 substituents selected from the group consisting of C₁-C₄ alkyl, C₁-C₄ alkoxy, halo, CF₃, and nitro;
- R^{3d} is H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, or heteroaryl(C₁-C₆ alkyl)-:
- R^{4d} and R^{5d} are independently H. C1-C4 alkoxy, NR^{2d}R^{3d}, halogen, NO₂, CN, CF₃, C1-C6 alkyl, C3-C6 alkenyl, C3-C7 cycloalkyl, C4-C11 cycloalkylalkyl, aryl, aryl(C1-C6 alkyl)- C2-C7 alkylcarbonyl, or arylcarbonyl;
- alternatively, when substituents on adjacent atoms, R^{4d} and R^{5d} can be taken together with the carbon atoms to which they are attached to form a 5-7 membered carbocyclic or 5-

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

7 membered heterocyclic aromatic or non-aromatic ring system, said carbocyclic or heterocyclic ring being optionally substituted with 0-2 groups selected from C₁-C₄ alkyl, C₁-C₄ alkoxy, halo, cyano, amino, CF₃, or NO₂;

$$-(CH_2)_n^d(CR^{7d}=CR^{8d})(CH_2)_m^d$$
-,

$$\hbox{-(CH$_2$)$}_n^d\hbox{O(CH$_2$)$}_m^d\hbox{-,}$$

$$-(CH_2)_n^d N(R^{6d})(CH_2)_m^d$$
-,

$$-(CH_2)_n^d C(=O)(CH_2)_m^d$$
-, or

$$\hbox{-(CH$_2$)$}_n{}^d S(O)_p{}^d (CH$_2$)_m{}^d \hbox{--};$$

wherein one or more of the methylene groups in U^{d} is optionally substituted with R^{7d} ;

Q^d is 1,2-phenylene, 1,3-phenylene, 2,3-pyridinylene, 3,4-pyridinylene, or 2,4-pyridinylene;

R^{6d} is H, C₁-C₄ alkyl, or benzyl;

R^{7d} and R^{8d} are independently H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, or heteroaryl(C₀-C₆ alkyl)-;

$$W^{d}$$
 is $-C(=O)-N(R^{13d})-(C(R^{12d})_{2})_{q}^{d}$ -;

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

$$x^{d}$$
 is $-C(R^{12d})(R^{14d})-C(R^{12d})(R^{15d})$ -;

alternatively, \boldsymbol{W}^{d} and \boldsymbol{X}^{d} can be taken together to be

$$- (CH_2)_q^dC (=0) -N N-R^{18d}$$

R^{12d} is H or C₁-C₆ alkyl;

d is 1, 2, 3, 4, or 5;

d' is 1-50;

W is independently selected at each occurrence from the group consisting of O, NH,

 $\label{eq:NHC} NHC(=O), C(=O)NH, NR^8C(=O), C(=O)N \ R^8, C(=O), C(=O)O, OC(=O), \\ NHC(=S)NH, NHC(=O)NH, SO_2, (OCH_2CH_2)_S, (CH_2CH_2O)_S', (OCH_2CH_2CH_2)_S'', \\ (CH_2CH_2CH_2O)_t, and (aa)_t';$

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

aa is independently at each occurrence an amino acid;

- Z is aryl substituted with 0-1 R¹⁰, C₃₋₁₀ cycloalkyl substituted with 0-1 R¹⁰, or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from the group consisting of N, S, and O and substituted with 0-1 R¹⁰;
- R^6 , R^6 a, R^7 , R^{7a} , and R^8 are independently selected at each occurrence from the group consisting of H, =O, COOH, SO₃H, C₁-C₅ alkyl substituted with 0-1 R^{10} , aryl substituted with 0-1 R^{10} , benzyl substituted with 0-1 R^{10} , and C₁-C₅ alkoxy substituted with 0-1 R^{10} , NHC(=O)R¹¹, C(=O)NHR¹¹, NHC(=O)NHR¹¹, NHR¹¹, R^{11} , and a bond to C_h;

k is 0 or 1; s is 0, 1, 2, 3, 4, or 5; s' is 0, 1, 2, 3, 4, or 5;

s" is 0, 1, 2, 3, 4, or 5;

t is s 0, 1, 2, 3, 4, or 5;

- A¹, A², A³, A⁴, A⁵, A⁶, A⁷, and A⁸ are independently selected at each occurrence from the group consisting of NR¹³, NR¹³R¹⁴, S, SH, S(Pg), OH, and a bond to L_n;
- E is a bond, CH, or a spacer group independently selected at each occurrence from the group the group consisting of C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, aryl substituted with 0-3 R¹⁷, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁷, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from the group consisting of N, S, and O and substituted with 0-3 R¹⁷;

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

 R^{13} and R^{14} are each independently selected from the group consisting of a bond to L_n , hydrogen, C_1 - C_{10} alkyl substituted with 0-3 R^{17} , aryl substituted with 0-3 R^{17} , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from the group consisting of N, S, and O and substituted with 0-3 R^{17} , and an electron, provided that when one of R^{13} or R^{14} is an electron, then the other is also an electron;

alternatively, R^{13} and R^{14} combine to form = $C(R^{20})(R^{21})$;

- $R^{17} \text{ is independently selected at each occurrence from the group consisting of a bond to L_n, $$ =O, F, Cl, Br, I, -CF_3, -CN, -CO_2R^{18}, -C(=O)R^{18}, -C(=O)N(R^{18})_2, -CH_2OR^{18}, $$ -OC(=O)R^{18}, -OC(=O)OR^{18a}, -OR^{18}, -OC(=O)N(R^{18})_2, -NR^{19}C(=O)R^{18}, $$ -NR^{19}C(=O)OR^{18a}, -NR^{19}C(=O)N(R^{18})_2, -NR^{19}SO_2N(R^{18})_2, -NR^{19}SO_2R^{18a}, $$ -SO_3H, -SO_2R^{18a}, -S(=O)R^{18a}, -SO_2N(R^{18})_2, -N(R^{18})_2, -NHC(=S)NHR^{18}, $$ =NOR^{18}, -C(=O)NHNR^{18}R^{18a}, -OCH_2CO_2H, and 2-(1-morpholino)ethoxy; $$ $$ $$ -OCH_2CO_2H, and 2-(1-morpholino)ethoxy; $$ $$ -OCH_2CO_2H, and 2-(1-morpholin$
- R^{18} , R^{18a} , and R^{19} are independently selected at each occurrence from the group consisting of a bond to L_n , H, and C_1 - C_6 alkyl;
- R²⁰ and R²¹ are independently selected from the group consisting of H, C₁-C₅ alkyl,
 -CO₂R²⁵, C₂-C₅ 1-alkene substituted with 0-3 R²³, C₂-C₅ 1-alkyne substituted with
 0-3 R²³, aryl substituted with 0-3 R²³, and unsaturated 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from the group consisting of N, S, and O and substituted with 0-3 R²³;

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

alternatively, R^{20} and R^{21} , taken together with the divalent carbon radical to which they are attached form:

R²² and R²³ are independently H or R²⁴;

alternatively, R²², R²³ taken together form a fused aromatic or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from the group consisting of N, S, and O;

 R^{24} is independently selected at each occurrence from the group consisting of -CO₂R²⁵, -C(=O)N(R²⁵)₂, -CH₂OR²⁵, -OC(=O)R²⁵, -OR²⁵, -SO₃H, -N(R²⁵)₂, and -OCH₂CO₂H; and,

 R^{25} is independently selected at each occurrence from the group the group consisting of H and C_1 - C_3 alkyl.

60. (New) A compound according to Claim 59, wherein:

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

R^{1de} is:

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

$$-U^{d} \xrightarrow{N} N^{H_{2}}$$

wherein the above heterocycles are optionally substituted with 0-2 substituents selected from the group consisting of NH₂, halogen, NO₂, CN, CF₃, C₁-C₄ alkoxy, C₁-C₆ alkyl, and C₃-C₇ cycloalkyl;

 U^d is $-(CH_2)_n$ -, $-(CH_2)_t^d Q^d$ (CH₂)_m - or $-C(=O)(CH_2)_n^d$ -1-, wherein one of the methylene groups is optionally substituted with R^{7d} ;

 R^{7d} is C1-C6 alkyl, C3-C7 cycloalkyl, C4-C11 cycloalkylalkyl, aryl, aryl(C1-C6 alkyl), heteroaryl, or heteroaryl(C1-C6 alkyl);

 R^{10d} is H, R^{1de} , C_1 -C4 alkoxy substituted with 0-1 R^{21d} , halogen, CO_2R^{17d} , $CONR^{17d}R^{20d}$, C_1 -C6 alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 -C7 cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_4 -C11 cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , or aryl(C_1 -C6 alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} :

 $R^{10\text{de}} \text{ is H, C}_{1}\text{-C4 alkoxy substituted with 0-1 R}^{21\text{d}}, \text{ halogen, CO}_{2}\text{R}^{17\text{d}}, \text{ CONR}^{17\text{d}}\text{R}^{20\text{d}},$ $C_{1}\text{-C6 alkyl substituted with 0-1 R}^{15\text{d}} \text{ or 0-1 R}^{21\text{d}}, C_{3}\text{-C7 cycloalkyl substituted}$ with 0-1 R $^{15\text{d}}$ or 0-1 R $^{21\text{d}}$, C4-C $_{11}$ cycloalkylalkyl substituted with 0-1 R $^{15\text{d}}$ or 0-1 R $^{21\text{d}}$, or aryl(C1-C6 alkyl)- substituted with 0-1 R $^{15\text{d}}$ or 0-2 R $^{11\text{d}}$ or 0-1 R $^{21\text{d}}$;

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

$$W^{d}$$
 is $-C(=O)-N(R^{13d})-$;

$$X^{d}$$
 is -CH(R^{14d})-CH(R^{15d})-;

$$R^{13}^{d}$$
 is H or CH3;

R^{14d} is:

H, C₁-C₁₀ alkyl, aryl, or heteroaryl, wherein said aryl or heteroaryl groups are optionally substituted with 0-3 substituents selected from the group consisting of C₁-C₄ alkyl, C₁-C₄ alkoxy, aryl, halo, cyano, amino, CF₃, and NO₂;

R^{15d} is H or R^{16d}:

R^{19d} is:

hydroxy, C1-C10 alkoxy,

methylcarbonyloxymethoxy-,

ethylcarbonyloxymethoxy-,

t-butylcarbonyloxymethoxy-,

cyclohexylcarbonyloxymethoxy-,

1-(methylcarbonyloxy)ethoxy-,

1-(ethylcarbonyloxy)ethoxy-,

1-(t-butylcarbonyloxy)ethoxy-,

1-(cyclohexylcarbonyloxy)ethoxy-,

i-propyloxycarbonyloxymethoxy-,

t-butyloxycarbonyloxymethoxy-,

1-(i-propyloxycarbonyloxy)ethoxy-,

1-(cyclohexyloxycarbonyloxy)ethoxy-,

1-(t-butyloxycarbonyloxy)ethoxy-,

dimethylaminoethoxy-,

diethylaminoethoxy-,

(5-methyl-1,3-dioxacyclopenten-2-on-4-yl)methoxy-,

(5-(t-butyl)-1,3-dioxacyclopenten-2-on-4-yl)methoxy-,

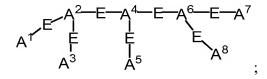
(1,3-dioxa-5-phenyl-cyclopenten-2-on-4-yl)methoxy-, or

1-(2-(2-methoxypropyl)carbonyloxy)ethoxy-;

R^{20d} is H or CH₃;

$$m^{d}$$
 is 0 or 1;

Ch is



 A^1 is OH, or a bond to L_n ;

 A^2 , A^4 , and A^6 are each N;

 A^3 , A^5 , and A^8 are each OH;

 A^7 is a bond to L_n or NH-bond to L_n ;

E is a C₂ alkyl substituted with 0-1 R¹⁷;

$$R^{17}$$
 is =0;

alternatively, Ch is

 A^1 is OH or a bond to L_n ;

 A^2 , A^3 and A^4 are each N;

 A^5 , A^6 and A^8 are each OH;

 A^7 is a bond to L_n ;

E is a C₂ alkyl substituted with 0-1 R¹⁷;

$$R^{17}$$
 is =0;

alternatively,
$$C_h$$
 is $A^{\uparrow} \stackrel{E-A^2}{\longrightarrow}$;

$$A^1$$
 is NH2 or N=C(R²⁰)(R²¹);

E is a bond;

$$A^2$$
 is NHR¹³;

R¹³ is a heterocycle substituted with R¹⁷, the heterocycle being selected from pyridine and pyrimidine;

 R^{17} is a bond to L_n, C(=O)NHR¹⁸ or C(=O)R¹⁸;

 R^{18} is a bond to L_n ;

$$R^{24}$$
 is $-CO_2R^{25}$, $-OR^{25}$, $-SO_3H$, or $-N(R^{25})_2$; and,

 R^{25} is independently selected at each occurrence from the group consisting of hydrogen and methyl.

61. (New) A compound according to Claim 60, wherein:

Application No.: 10/770,380
Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

R1de is

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

wherein the above heterocycles are optionally substituted with 0-2 substituents selected from the group consisting of NH₂, halogen, NO₂, CN, CF₃, C₁-C₄ alkoxy, C₁-C₆ alkyl, and C₃-C₇ cycloalkyl.

- 62. (New) A compound according to Claim 59, wherein the compound is:
- 2-(((4-(4-(((3-(2-(2-(3-((6-((1-aza-2-(2-sulfophenyl)vinyl)amino)(3-pyridyl))carbonylamino)propoxy)ethoxy)ethoxy)propyl)amino)sulfonyl)-phenyl)phenyl)sulfonyl)amino)-3-((1-(3-(imidazole-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)propanoic acid;
- 2-(2-aza-2-((5-(N-(1,3-bis(3-(2-(2-(3-(((4-(((1-carboxy-2-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)ethyl)amino)sulfonyl)-phenyl)sulfonyl)amino)propoxy)ethoxy)ethoxy)propyl)carbamoyl)propyl)carbamoyl)(2-pyridyl))amino)vinyl)benzenesulfonic acid;
- 2-((6-((1-aza-2-(sulfophenyl)vinyl)amino)(3-pyridyl))carbonylamino)-4-(N-(3-(2-(2-(3-(((4-((1-carboxy-2-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))-carbonylamino)ethyl)amino)sulfonyl)phenyl)phenyl)sulfonyl)amino)propoxy)-ethoxy)propyl)carbamoyl)butanoic acid;
- 3-((1-(3-(imidazole-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)-2-(((4-(4-(((3-(2-(2-(3-(2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl)-acetylamino)propoxy)ethoxy)ethoxy)propyl)amino)sulfonyl)-phenyl)phenyl)sulfonyl)amino)propanoic acid;
- 2-(6-((6-((1-aza-2-(2-sulfophenyl)vinyl)-amino)(3-pyridyl))carbonylamino)hexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)-propanoic acid;

DOCKET NO.: DM-6999 (BMS-2594) **Application No.:** 10/770,380 **Office Action Dated:** June 16, 2006

- 2-((6-((1-aza-2-(2-sulfophenyl)vinyl)-amino)(3-pyridyl))carbonylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)propanoic acid;
- [2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-Glu(2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid)(2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid);
- [2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-Glu-bis-[Glu(2-(6-Aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid)(2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid)];
- 2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)-1-cyclododecyl)acetyl-{2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid};
- 2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)-1-cyclododecyl)acetyl-Glu{2-(6-Aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid} {2-(6-Aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid};

Page 43 of 51

DOCKET NO.: DM-6999 (BMS-2594) **Application No.:** 10/770,380 **Office Action Dated:** June 16, 2006

Application No.: 10/770,380 **Office Action Dated:** June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

$$CO_2H$$
 CO_2H
 CO_2

2-(((4-(3-(N-(3-(2-(2-(3-(2-(1,4,7,10-tetraaza-4,7,10-

tris(carboxymethyl)cyclododecylacetylamino)-6aminohexanoylamino)propoxy)ethoxy)ethoxy)propyl)carbamoyl)propoxy)-2,6dimethylphenyl)sulfonyl)amino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5yl))carbonylamino)propionic acid salt;

Application No.: 10/770,380 **Office Action Dated:** June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

2-({[4-(3-{N-[2-((2R)-3-Sulfo-2-{2-[1,4,7,10-tetraaza-4,7,10-

tris(carboxymethyl)cyclododecyl]acetylamino}propyl)ethyl]carbamoyl}propoxy)-2,6-dimethylphenyl]sulfonyl}amino)(2S)-3-({1-[3-(imidazol-2-ylamino)propyl](1H-indazol-5-yl)}carbonylamino)propanoic Acid;

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

- 2-[({4-[4-({[2-((2R)-3-Sulfo-2-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]-acetylamino}propyl)ethyl]amino}sulfonyl)phenyl]phenyl}sulfonyl)amino](2S)-3-({1-[3-(imidazol-2-ylamino)propyl](1H-indazol-5-yl)}carbonylamino)propanoic Acid;
- (4S)-4-(N-{1-[N-(2-{4-[4-({[(1S)-1-carboxy-2-({1-[3-(2-pyridylamino)propyl](1H-indazol-5-yl)}carbonylamino)ethyl]amino}sulfonyl)-3,5-dimethylphenoxy]butanoylamino}ethyl)carbamoyl]-3-carboxypropyl}carbamoyl)-4-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]acetylamino}butanoicacid;
- (4S)-4-(N-{1-[N-(2-{4-[4-({[(1S)-1-carboxy-2-({1-[3-(imidazol-2-ylamino)propyl](1H-indazol-5-yl)}carbonylamino)ethyl]amino}sulfonyl)-3,5-dimethylphenoxy]butanoylamino}ethyl)carbamoyl]-3-carboxypropyl}carbamoyl)-4-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]acetylamino}butanoicacid;
- $(4S)-4-\{N-[(1S)-1-(N-\{1,3-bis[N-(2-\{4-[4-(\{[(1S)-1-carboxy-2-(\{1-[3-(imidazol-2-ylamino)propyl](1H-indazol-5-yl)\}carbonylamino)ethyl]amino\} sulfonyl)-3,5-ylamino (2-\{4-[4-(\{[(1S)-1-carboxy-2-(\{1-[3-(imidazol-2-ylamino)propyl](1H-indazol-5-yl)\}carbonylamino)ethyl]amino)ethylamino(ethylamino)ethylamino(ethylamino)ethylamino(ethylamino)ethylamino(ethylamino)ethylamino(ethylamino)ethylamino(ethylamino)ethylamino(ethylamino)ethylamino(ethylamino)ethylamino(ethylamino)ethylamino(ethylamino)ethylamino(ethylamino)ethylamino(ethylamino)ethylamino(ethylamino)ethylamino(eth$

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

DOCKET NO.: DM-6999 (BMS-2594) **Application No.:** 10/770,380 **Office Action Dated:** June 16, 2006

dimethylphenoxy]butanoylamino}ethyl)carbamoyl]propyl}carbamoyl)-3-carboxypropyl]carbamoyl}-4-(6-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]acetylamino} hexanoylamino)butanoic acid;

- (4S)-4-(N-{1-[N-(2-{4-[4-({[(1S)-1-carboxy-2-({1-[3-(3,4,5,6-tetrahydropyrimidin-2-ylamino)propyl](1H-indazol-5-yl)}carbonylamino)ethyl]amino}sulfonyl)-3,5-dimethylphenoxy]butanoylamino}ethyl)carbamoyl]-3-carboxy propyl}carbamoyl)-4-{2-[1,4,7,10-tetraaza-4,7,10-tris (carboxymethyl)cyclododecyl]acetylamino}butanoic acid;
- (4S)-4-(N-{1-[N-(2-{4-[4-({[(1S)-1-carboxy-2-({1-methyl-3-[3-(2-3,4,5,6-tetrahydropyridylamino)propyl] (1H-indazol-6-yl)}carbonylamino)ethyl]amino}sulfonyl)-3,5-dimethylphenoxy]butanoylamino}ethyl)carbamoyl]-3-carboxypropyl}carbamoyl)-4-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]acetylamino}butanoicacid;
- (4S)-4-(N-{(1S)-1-[N-(2-{4-[4-({[(1S)-1-carboxy-2-({1-[2-(2-3,4,5,6-tetrahydropyridylamino)ethyl] (1H-indazol-5-yl)}carbonylamino)ethyl]amino}sulfonyl)-3,5-dimethylphenoxy]butanoylamino}ethyl)carbamoyl]-3-carboxy propyl}carbamoyl)-4-{2-[1,4,7,10-tetraaza-4,7,10-tris (carboxymethyl)cyclododecyl]acetylamino}butanoic acid;
- (2S)-2-{[(2,6-dimethyl-4-{3-[N-(2-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]acetyl-amino}ethyl)carbamoyl]propoxy}phenyl)sulfonyl]amino}-3-({2-[2-(2-3,4,5,6-tetrahydropyridylamino)ethyl](2-hydro-1H-indazol-5-yl)}carbonylamino)propanoic acid;

Application No.: 10/770,380

Office Action Dated: June 16, 2006

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

- (4S)-4-{N-[(1S)-1-(N-{2-[({4-[4-({[(1S)-1-carboxy-2-({1-[2-(2-3,4,5,6-tetrahydropyridylamino)ethyl] (1H-indazol-5-yl)}carbonylamino)ethyl]amino}sulfonyl)phenyl]

 phenyl}sulfonyl)amino]ethyl}carbamoyl)-3-carboxypropyl] carbamoyl}-4-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxy-methyl)cyclododecyl]acetylamino}butanoic acid;
- (4S)-4-{N-[(1S)-1-(N-{2-[({4-[4-({[(1S)-1-carboxy-2-({1-[3-(3,4,5,6-tetrahydropyrimidin-2-ylamino) propyl](1H-indazol-5-yl)}carbonylamino)ethyl]amino}sulfonyl) phenyl]phenyl}sulfonyl)amino]ethyl}carbamoyl)-3-carboxy propyl]carbamoyl}-4-{2-[1,4,7,10-tetraaza-4,7,10-tris (carboxymethyl)cyclododecyl]acetylamino}butanoic acid;
- (2S)-3-({3-[(imidazol-2-ylamino) methyl]-1-methyl(1H-indazol-6-yl)} carbonylamino)-2-({[4-(4-{[(2-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl) cyclododecyl]acetylamino}ethyl)amino]sulfonyl} phenyl)phenyl]sulfonyl} amino)prop anoic acid;
- 3-[(7-{3-[(6-{[(1E)-1-aza-2-(2-sulfophenyl)vinyl]amino}(3-pyridyl))carbonylamino]propoxy}-1-[3-(imidazol-2-ylamino)propyl](1H-indazol-5-yl))-carbonylamino](2S)-2-{[(2,4,6-trimethylphenyl)sulfonyl]-amino}propanoic acid; or
- 3-{[1-[3-(imidazol-2-ylamino)propyl]-7-(3-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]-acetylamino}propoxy)(1H-indazol-5-yl)]carbonylamino}-2-{[(2,4,6-trimethylphenyl)sulfonyl]amino}propanoic acid;

or a pharmaceutically acceptable salt form thereof.